Twenty-Year Trends in the Incidence and Outcome of Cardiogenic Shock in AMIS Plus Registry

Hunziker, Lukas ; Radovanovic, Dragana ; Jeger, Raban ; Pedrazzini, Giovanni ; Cuculi, Florim ; Urban, Philip ; Erne, Paul ; Rickli, Hans ; Pilgrim, Thomas

Abstract: BACKGROUND Long-term trends of the incidence and outcome of cardiogenic shock (CS) patients are scarce. We analyze for the first time trends in the incidence and outcome of CS during a 20-year period in Switzerland. METHODS AND RESULTS The AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry enrolls patients with acute myocardial infarction from 83 hospitals in Switzerland. We analyzed trends in the incidence, treatment, and in-hospital mortality of patients with CS enrolled between 1997 and 2017. The impact of revascularization strategy on outcome was assessed for the time period 2005 to 2017. Among 52 808 patients enrolled, 963 patients were excluded because of missing data and 51 842 (98%) patients remained for the purpose of the present analysis. Overall, 4090 patients (7.9%) with a mean age of 69.6±12.5 years experienced acute myocardial infarction complicated by CS. Overall, rates of CS declined from 8.7% to 7.3% between 1997 and 2017 (P for trend, <0.001; 1997-2006 versus 2007-2017). We observed a decrease in CS developing during hospitalization from 7.8% to 3.5% in the period 1997 to 2006 compared with 2007 to 2017 (P for trend, <0.001), which was partially offset by an increase in CS on admission between 2006 and 2017 (2.5% [1997-2006] to 4.6% [2007-2017]; P for trend, <0.001). In-hospital mortality declined from 62.2% in 1997 to 36.3% in 2017 (P<0.001 for temporal trend). Percutaneous coronary intervention was the strongest independent predictor for survival (odds ratio, 0.36; CI, 0.28-045; P<0.001). Among patients with acute myocardial infarction and multivessel disease, multivessel percutaneous coronary intervention was associated with an increased risk of in-hospital mortality (odds ratio, 1.88; 95% CI, 1.59-2.21) and was an independent predictor for the development of CS during hospitalization (odds ratio, 1.93; 95% CI, 1.62-2.30). CONCLUSIONS Rates of CS declined between 1997 and 2017 driven by a reduction of CS developing during hospitalization. In-hospital mortality from CS declined from 62.8% (1997) to <40% (2017). Multivessel percutaneous coronary intervention was associated with an increased risk of mortality and the development of CS during hospitalization.

DOI: https://doi.org/10.1161/CIRCINTERVENTIONS.118.007293

Outcome of Cardiogenic Shock in AMIS Plus Registry. Circulation. Cardiovascular Interventions, 12(4):e007293.
DOI: https://doi.org/10.1161/CIRCINTERVENTIONS.118.007293

Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Twenty-Year Trends in the Incidence and Outcome of Cardiogenic Shock in AMIS Plus Registry

Lukas Hunziker, MD
Dragana Radovanovic, MD
Raban Jeger, MD
Giovanni Pedrazzini, MD
Florim Cuculi, MD
Philip Urban, MD
Paul Erne, MD
Hans Rickli, MD
Thomas Pilgrim, MD
the AMIS Plus Registry Investigators*

BACKGROUND: Long-term trends of the incidence and outcome of cardiogenic shock (CS) patients are scarce. We analyze for the first time trends in the incidence and outcome of CS during a 20-year period in Switzerland.

METHODS AND RESULTS: The AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry enrolls patients with acute myocardial infarction from 83 hospitals in Switzerland. We analyzed trends in the incidence, treatment, and in-hospital mortality of patients with CS enrolled between 1997 and 2017. The impact of revascularization strategy on outcome was assessed for the time period 2005 to 2017. Among 52 808 patients enrolled, 963 patients were excluded because of missing data and 51 842 (98%) patients remained for the purpose of the present analysis. Overall, 4090 patients (7.9%) with a mean age of 69.6±12.5 years experienced acute myocardial infarction complicated by CS. Overall, rates of CS declined from 8.7% to 7.3% between 1997 and 2017 (*P* for trend, <0.001; 1997–2006 versus 2007–2017). We observed a decrease in CS developing during hospitalization from 7.8% to 3.5% in the period 1997 to 2006 compared with 2007 to 2017 (*P* for trend, <0.001), which was partially offset by an increase in CS on admission between 2006 and 2017 (2.5% [1997–2006] to 4.6% [2007–2017]; *P* for trend, <0.001). In-hospital mortality declined from 62.2% in 1997 to 36.3% in 2017 (*P*<0.001 for temporal trend). Percutaneous coronary intervention was the strongest independent predictor for survival (odds ratio, 0.36; CI, 0.28–045; *P*<0.001). Among patients with acute myocardial infarction and multivessel disease, multivessel percutaneous coronary intervention was associated with an increased risk of in-hospital mortality (odds ratio, 1.88; 95% CI, 1.59–2.21) and was an independent predictor for the development of CS during hospitalization (odds ratio, 1.93; 95% CI, 1.62–2.30).

CONCLUSIONS: Rates of CS declined between 1997 and 2017 driven by a reduction of CS developing during hospitalization. In-hospital mortality from CS declined from 62.8% (1997) to <40% (2017). Multivessel percutaneous coronary intervention was associated with an increased risk of mortality and the development of CS during hospitalization.

VISUAL OVERVIEW: A visual overview is available for this article.

Key Words: acute coronary syndrome ■ humans ■ incidence ■ shock ■ Switzerland

https://www.ahajournals.org/journal/circinterventions

WHAT IS KNOWN

- Long-term trends of incidence and outcome of cardiogenic shock (CS) patients are scarce—a reduction in CS-associated mortality since the late nineties has been reported; the incidence of CS remained unchanged.
- Multivessel percutaneous coronary intervention is not recommended in CS and controversial in acute myocardial infarction.

WHAT THE STUDY ADDS

- We confirm a reduction of CS-associated in-hospital mortality in the last 20 years from >60% in 1997 to <40% in 2017.
- The incidence of CS developing during hospitalization further declined during the last 20 years, whereas the incidence of CS on admission increased.
- Multivessel percutaneous coronary intervention in acute myocardial infarction was associated with an increased risk of mortality and the development of CS during hospitalization.

Long-term trends of the incidence and outcome of cardiogenic shock (CS) patients are scarce. The incidence of CS varies substantially among available long-term studies and depends on the region and time period studied. Several studies have shown a variable decrease in the rates of CS ranging from 1.8% to 1.4% between 2000 and 2013 in a study from Israel,[1] from 12% in 1995 to 4% in 2012[2] or from 3.4% in 1992 to 2.6% in 2008.[3] In summary, a decrease in the incidence of CS is generally documented after the late 1990's.[4] While in the last decade (2001–2011), a relatively stable incidence of 3.7%[5] and 5.2% has been reported,[6,7] 2 recent studies document an increasing incidence of CS during the last decade (2003–2010) from 7.9 to 10.1 in patients ST-segment–elevation myocardial infarction (STEMI)[8] and non-STEMI patients.[9] In all studies, a consistent decrease of mortality after CS was observed since the nineties.[3,4,10]

Previously, the AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry reported the incidence and mortality of CS in Switzerland during the period between 1997 and 2006.[11] Since 2006, several trials have been published that changed treatment strategies and management of CS. Currently, patients are treated with newer generation drug-eluting stents, and the use of bare metal stents has declined. Early revascularization has emerged as a standard therapy for CS. On the contrary, the intra-aortic balloon pump (IABP)-shock II trial showed a lack of survival benefit with the use of the IABP in patients with CS with a 40% mortality at 30 days and a 50% mortality at 12 months in both groups—IABP versus standard medical therapy.[12,13] Other mechanical circulatory devices such as axial flow pump (Impella, Abiomed) or the venous-arterial extracorporal membrane oxygenation (ECMO) have emerged, although no large randomized trials are available supporting the use of any of these devices. The recently published CULPRIT-shock trial failed to show a benefit with the multivessel treatment strategy[14–16] versus the culprit vessel–only treatment strategy in CS.[17]

The AMIS Plus Registry is a Swiss nationwide cohort study collecting data on hospital admissions for acute myocardial infarction (AMI) since 1997. The aim of this study is first to analyze temporal trends in the incidence and mortality of CS over the last 20 years and to assess the impact of culprit versus multivessel revascularization in this real-world registry. In addition, predictors of mortality and of development of CS during hospitalization are analyzed.

METHODS

AMIS Plus Registry

Since 1997, 83 of the 106 acute cardiac care hospitals in Switzerland have participated in the AMIS Plus Registry.[11] All participating hospitals have either a catheterization laboratory or direct access to a center providing percutaneous coronary intervention (PCI) within 90 minutes for all patients.

Data Availability Statement: the authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. Individual data used for the construction of the AMIS Plus Registry are property of the hospitals participating in the AMIS registry and may only be made available by each hospital's principal investigator and steering committee. This also applies to derivatives such as the analysis files used for this study. However, after approval of the AMIS Plus steering committee and subsequent negotiation of an individual AMIS plus module contract with the AMIS Plus steering committee, analysis files can be handed over to other researchers. Requests must be submitted to Prof Paul Erne (President of the AMIS Plus Steering Committee; paul.erne@ernenet.ch) and Dr Dragana Radovanovic (Head of Data Center AMIS Plus; dragana.radovanovic@uzh.ch).

Ethics

The Swiss Societies of Internal Medicine, Cardiology, and Intensive Care Medicine founded the AMIS Plus Registry project. A steering committee that includes members of the founding medical societies guides the project. This study complied with the Declaration of Helsinki regarding investigations on humans and was approved by the Swiss National Ethical Committee for Clinical Studies, the Board for Data Security and all cantonal ethic committees approved the registry.

Data Collection

Investigators at participating centers collect data for the registry by using identical web-based data entry systems. The case record form has 240 items that address medical history, cardiovascular risk factors, symptoms, initial out-of-hospital management, clinical presentation, early in-hospital management,

reperfusion therapy, hospital course, diagnostic tests used or planned, length of stay, and discharge medication and destination. A data coordinating center checks data for plausibility and consistency. Central data monitors returned incomplete questionnaires to the participating centers for completion (19% in 2003). This approach helped to minimize data loss and warrant a consistent data quality (<1% overall and 0% for therapeutic interventions).[18]

Patient Enrollment

Patients were enrolled in the registry if their final diagnosis met 1 of the 3 following criteria: AMI, defined as symptoms or electrocardiographic changes compatible with AMI and cardiac markers (either creatine kinase MB fraction at least twice the upper limit of normal or troponin I or T above individual hospital cutoff levels for myocardial infarction). Cases of unstable angina were excluded. In this study, we included all patients with AMI (non-STEMI and STEMI) entered in the AMIS Plus Registry between January 1, 1997, and December 31, 2017, from the participating hospitals.

Charlson Comorbidity Index was measured since 2002. Data for multivessel disease treatment strategies were available since 2005. Of 18949 patients with multivessel disease assessed between 2005 and 2017 with AMI, 15916 (84%) data with respect to multivessel versus culprit vessel treatment were available. Data of Impella and ECMO usage were collected since 2013.

Definitions

Patients who had ST-segment elevation or new left bundle branch block on their initial ECG were classified as ST-segment–elevation AMI. We classified patients who had ST-segment depression or T-wave abnormalities in the absence of ST-segment elevation on the initial ECG as non–ST-segment–elevation AMI. We defined CS at admission and during hospitalization in all participating centers by using the Killip definition of hypotension (systolic blood pressure <90 mm Hg) and evidence of hypoperfusion (oliguria, cyanosis, and cold extremities).[19]

Statistical Analysis

The results are presented as percentages for categorical variables. Data are analyzed using the nonparametric Pearson χ^2 test or Fisher exact test where appropriate. In the case of missing data, instead of an imputation procedure, we provide the number of patients with a characteristic to number of patients with available data (n). Continuous normally distributed variables are expressed as means±1 SD and compared using the Student 2-tailed unpaired *t* test. Continuous nonnormally distributed variables are expressed as median and interquartile ranges and analyzed using the Mann-Whitney *U* test. Univariable and multivariable binary logistic regressions were used to analyze trends of mortality over admission years. Variable selection was based on prior studies, experience, and clinical knowledge. Explanatory variables were CS at admission, CS developing during hospitalization, age, sex, STEMI, and performed PCI. Model fit was assessed using the Hosmer-Lemeshow test. The results of logistic regression are reported as odds ratios (ORs) with a 95% CI. A *P* value of <0.01 was considered significant. SPSS software (version 23; SPSS, Inc, Chicago, IL) was used for statistical analysis.

RESULTS

Patients

From January 1997 to December 2017, 52805 patients with AMI were included in the AMIS Plus Registry (Figure 1). Four thousand ninety patients (7.7%) presented with CS, of whom 1907 patients (3.6% of those with AMI and 46.6% of those with CS) had CS on admission and 2183 patients (4.1% of those with AMI and 53.4% of those with CS) developed CS during hospitalization.

Baseline risk for cardiovascular disease (dyslipidemia, hypertension, diabetes mellitus, and renal disease but not smoking) was higher among patients with CS than among those without (Table 1); specifically, patients with CS were older, more likely to be women, and had a higher incidence of atrial fibrillation. The incidence of resuscitation was 30.1% among patients with CS compared with 3.3% in patients with AMI (*P*<0.001).

The presence of a Charlson Comorbidity Index >1, was higher in the CS population compared with AMI patients (22.4%–35.9%; *P*<0.001) and also higher in patients who acquired CS during hospitalization (31.9%–40.5%; *P*<0.001).

Therapeutic Interventions

Patient with CS less often received immediate medical treatment such as aspirin, P2Y12 inhibitors, β-blocker, nitrate, ACE (angiotensin-converting enzyme) inhibitor/ARB (angiotensin II receptor blocker), and statins

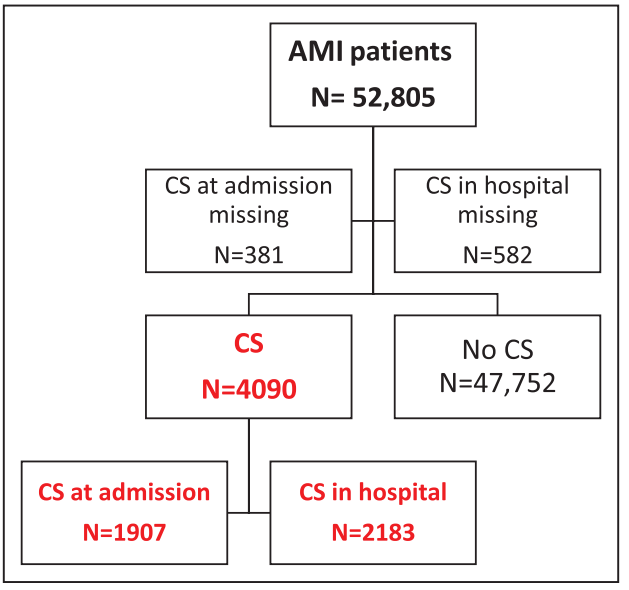

Figure 1. Flowchart of patients included in the acute myocardial infarction study.
AMI indicates acute myocardial infarction; CS, cardiogenic shock.

Table 1. Baseline Characteristics of Patients With Acute Myocardial Infarction According to CS (n=51 842)

n (%)	No CS (n=47 752)	CS (n=4090)	*P* Value	CS at Admission (n=1907)	CS During Hospitalization (n=2183)	*P* Value
Age, y; mean (SD)	65.8 (13.2)	69.6 (12.5)	<0.001	67.2 (12.6)	71.7 (12.0)	0.001
Sex: female (%)	12 631/47 752 (26.5)	1263/4090 (30.9)	<0.001	506/1907 (26.5)	757/2183 (34.7)	<0.001
Resuscitation prior admission (%)	1569/47 549 (3.3)	1223/4059 (30.1)	<0.001	959/1895 (50.6)	264/2164 (12.2)	<0.001
Delay, min (symptoms on admission); median (IQR)	230 (115–660)	165 (84–483)	<0.001	110 (67–254)	240 (115–781)	<0.001
Vital signs at admission, mean (SD)						
Systolic blood pressure, mm Hg	138.4 (27.1)	111.7 (31.0)	<0.001	101.3 (29.8)	120.4 (29.2)	<0.001
Diastolic blood pressure, mm Hg	80.6 (16.8)	67.4 (21.5)	<0.001	62.0 (23.1)	71.8 (19.0)	<0.001
Heart rate, bpm	78.2 (19.2)	89.5 (28.2)	<0.001	90.9 (30.5)	88.4 (26.0)	0.005
STEMI (%)	27 466/47 752 (57.5)	3027/4090 (74.0)	<0.001	1405/1907 (73.7)	1622/2183 (74.3)	0.67
NSTEMI (%)	20 286/47 752 (42.5)	1063/4090 (26.0)	<0.001	502/1907 (26.3)	561/2183 (25.7)	0.67
Killip classes	n=47 419	n=4030	<0.001	n=1907	n=2123	<0.001
Class I	39 993 (84.3)	1111 (27.6)		0	1111 (52.3)	
Class II	5883 (12.4)	630 (15.6)		0	630 (29.7)	
Class III	1540 (3.2)	382 (9.5)		0	382 (18.0)	
Class IV	0	1907 (47.3)		1907 (100)	0	
Risk factors/history of the following						
Smoking (%)	17 202/43 710 (39.4)	1285/3173 (40.5)	0.21	666/1343 (49.6)	619/1830 (33.8)	<0.001
Dyslipidemia (%)	25 267/42 870 (58.9)	1681/3226 (52.1)	<0.001	772/1438 (53.7)	909/1788 (50.8)	0.11
Hypertension (%)	27 223/45 700 (59.6)	2300/3563 (64.6)	<0.001	1024/1579 (64.9)	1276/1984 (64.3)	0.75
Diabetes mellitus (%)	9121/46 045 (19.8)	1086/3634 (29.9)	<0.001	465/1604 (29.0)	621/2030 (30.6)	0.31
Obesity (%), BMI >30	8363/40 509 (20.6)	550/2928 (18.8)	0.016	236/1375 (17.2)	314/1553 (20.2)	0.037
Coronary artery disease (%)	14 962/44 830 (33.4)	1267/3547 (35.7)	0.005	535/1679 (31.9)	732/1868 (39.2)	<0.001
Renal disease* (%)	2647/39 397 (6.7)	364/2776 (13.1)	<0.001	155/1487 (10.4)	209/1289 (16.2)	<0.001
Cancer diseases* (%)	2153/39 396 (5.5)	215/2795 (7.7)	<0.001	106/1506 (7.0)	109/1289 (8.5)	0.18
Charlson Comorbidity Index >1* (%)	8826/39 396 (22.4)	996/2776 (35.9)	<0.001	474/1487 (31.9)	522/1289 (40.5)	<0.001

BMI indicates body mass index; CS, cardiogenic shock; IQR, interquartile range; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

*Available since 2002.

(Table 2). Conversely, diuretics and vasopressors agents were more often applied in CS patients. Coronary angiography was immediately performed only in 61% of patients with CS (in 75.8% in CS on admission and 48.4% in CS during hospitalization) compared with 71.5% in the overall AMI population. A total of 27% of patients with CS received an IABP with no difference among patients who presented with CS on admission or developed CS during hospitalization. In summary, 9.8% of patients received an ECMO or an axial flow pump device such as an Impella (data collected since 2013). Door-to-balloon time was documented in 84% of patients with CS. Median time was 64 minutes (range, 26–135 minutes). Invasive mechanical ventilation was introduced in 44.6% of patients with CS and 7.7% (data available since 2005) received non-invasive mechanical ventilation. In 16.5% of patients with CS, a hypothermia protocol (data available since 2009) was applied (Table 2).

Treatment of CS With Multivessel Disease and Predictors of Mortality

Data with respect to treatment strategies of multivessel disease were collected since 2005. In 15 916 of 18 949 patients, data of multivessel disease and treatment strategy were available of whom 1225 patients presented with a CS. In 804 (65.6%) patients, the culprit vessel only was treated, and in 421 (34.4%), multivessel revascularization was performed. There was no difference with respect to crude mortality whether the culprit vessel–only or multivessel PCI was performed (39.1% versus 40.9% mortality; *P*=0.54; Table 2). In the CS population with multivessel disease (n=1225), multivariable logistic regression models including age, sex, and multivessel PCI did not reveal to be an independent predictor of mortality (OR, 1.12; 95% CI, 0.89–1.44). In contrast, predictor analysis of all AMI patients with multivessel disease (n=15 916/18 946) including age, sex, STEMI, and multivessel PCI was

Table 2. Immediate Therapies (Within the First 24 Hours) of Acute Myocardial Infarction Patients According to CS (N=51,842)

n (%)	No CS (n=47752)	CS (n=4090)	*P* Value	CS at Admission (n=1907)	CS During Hospitalization (n=2183)	*P* Value
Aspirin (%)	45611/47619 (95.8)	3559/4025 (88.5)	<0.001	1642/1867 (87.9)	1917/2158 (88.8)	0.40
P2Y12 inhibitor (%)	34039/47520 (71.6)	2198/4016 (54.7)	<0.001	1204/1862 (64.7)	994/2154 (46.1)	<0.001
GPIIb/IIIa inhibitors (%)	10410/42595 (24.4)	810/3336 (24.3)	0.85	396/1726 (22.9)	414/1610 (25.7)	0.063
Beta blocker (%)	31127/47336 (65.8)	1260/3989 (31.6)	<0.001	421/1841 (22.9)	839/2148 (39.1)	<0.001
Nitrate (%)	26867/47105 (57.0)	1698/3992 (42.5)	<0.001	540/1840 (29.3)	1158/2152 (53.8)	<0.001
ACEI/ARB (%)	25129/47219 (53.2)	1038/3972 (26.1)	<0.001	404/1833 (22.0)	634/2139 (29.6)	<0.001
Calcium channel blocker (%)	4432/46957 (9.4)	189/3974 (4.8)	<0.001	66/1834 (3.6)	123/2140 (5.7)	0.002
Diuretic (%)	6554/32738 (20.0)	824/2444 (33.7)	<0.001	427/1464 (29.2)	397/980 (40.5)	<0.001
Statin (%)	30951/40207 (77.0)	1511/3025 (50.0)	<0.001	803/1670 (48.1)	708/1355 (52.3)	0.023
Vasopressor (%)	1616/32600 (5.0)	1362/2453 (55.5)	<0.001	896/1475 (60.7)	466/978 (47.6)	<0.001
Coronary angiography (%)	34156/47752 (71.5)	2502/4089 (61.2)	<0.001	1445/1906 (75.8)	1057/2183 (48.4)	<0.001
PCI (%)	33264/46860 (71.0)	2443/4030 (60.6)	<0.001	1413/1874 (75.4)	1030/2156 (47.8)	<0.001
IABP(%)	855/47008 (1.8)	1079/3993 (27.0)	<0.001	519/1855 (28.0)	560/2138 (26.2)	0.21
ECMO/Impella (%)*	15/8488 (0.2)	74/757 (9.8)	<0.001	45/481 (9.4)	29/276 (10.5)	0.61
Invasive mechanical ventilation (%)	1995/47319 (2.3)	1801/4035 (44.6)	<0.001	933/1876 (49.7)	868/2159 (40.2)	<0.001
Non-invasive mechanical ventilation (%)†	396/33517 (1.2)	193/2522 (7.7)	<0.001	79/1510 (5.2)	114/1012) (11.3)	<0.001
Cooling of body temp (%)‡	25/4594 (0.5)	63/381 (16.5)	<0.001	59/259 (22.8)	4/122 (3.3)	<0.001

Culprit / Multivessel PCI n/N (%)	No CS (n=14691)	*P* Value	CS (n=1225)	*P* Value	CS at Admission (n=735)	*P* Value	CS During Hospitalization (n=490)	*P* Value
Culprit vessel treated§ Multivessel treated§	11321 (77.1%) 3370 (22.9%)	<0.001	804 (65.6%) 421 (34.4%)	<0.001	470 (63.9%) 265 (36.1%)		334 (68.2%) 156 (31.8%)	0.14
Mortality culprit PCI Mortality multivessel PCI	154 (1.4%) 68 (2%)	0.007	314 (39.1%) 172 (40.9%)	0.54	176 (37.4%) 107 (40.4%)	0.48	138 (41.3%) 65 (41.7%)	1.0

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotension II receptor antagonist; CS, cardiogenic shock; ECMO, extracorporal membrane oxygenation; P2Y12 inhibitors, clopidogrel, prasugrel or ticagrelor; PCI, percutaneous coronary intervention.

*Available since 2013.

†Available since 2005.

‡Available since 2009.

§Available since 2005.

identified as an independent predictor of mortality with an OR of 1.88 (95% CI, 1.59–2.21). In addition, multivessel PCI in AMI patients with multivessel disease was also an independent predictor for CS developing during hospitalization (OR, 1.93; 95% CI, 1.62–2.30).

Temporal Trends

Between 1997 and 2017, rates of CS decreased from 8.7% (1997–2006) to 7.3% (2007–2017; *P*<0.001; Figure 2). Compared with the previous time period of 1997 to 2006, the incidence of CS developing during hospitalization declined from 7.8% (1997–2006) to 3.5% (1997–2017; *P*<0.001), whereas the rates of CS on admission increased form 2.5% in 1997 to 2006 to 4.6% (*P*<0.001) in 2007 to 2017.

Rates of immediate medical therapy increased in the decade 2007 to 2017 compared to the decade 1997 to 2006, for aspirin from 94.2% to 96.0% (*P*<0.001), for P2Y12 from 47.5% to 87.9% (*P*<0.001), and for statins from 71.8% to 76.7% (*P*<0.001). Similar, rates of coronary angiography and PCI increased from 40.2% in 1997 to 2006 to 80% in the time period of 2007 to 2017 (*P*<0.001). Between 2007 and 2017, the use of ECMO/Impella (data available since 2013) increased, whereas rates of IABP implantation have remained stable. Need for coronary artery bypass graft surgery (10%) and multivessel PCI (2007: 35.4% and 2017: 33.8%; *P*=0.87) remained stable (Figure 3).

In-Hospital Complication and Outcome

The overall mortality in patients with CS between 1997 and 2017 was 49.2%, with a higher mortality rate in patients acquiring CS during hospitalization compared with AMI patients with CS on admission (53.5% versus 44.4%; *P*<0.001; Table 3). However, mortality rate in all CS patients was 62.8% in 1997 and declined to 46.8% in 2006 to 36.3% in 2017 (*P* <0.001 for temporal trend; Figure 4).

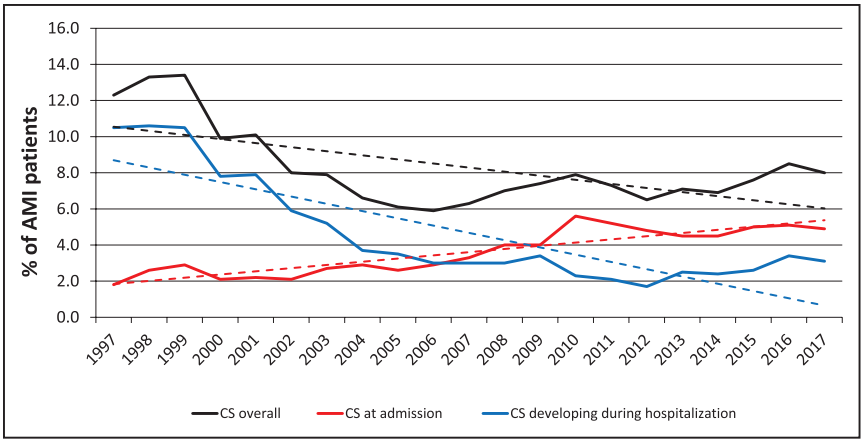

Figure 2. Trends in the incidence of overall cardiogenic shock (CS), CS at admission, and CS developing during hospitalization in patients with acute myocardial infarction (AMI; n=51842).
Percentage in the table indicates percentage of overall CS. Dotted lines indicate trendlines.

Rates of reinfarction (3.0% versus 10.8%; *P*<0.001) and major adverse cardiac events (47.3% versus 56.8%; *P*<0.001) were significantly lower in CS on admission compared with CS acquired during hospitalization. No difference was observed with respect to bleeding, cerebrovascular events, length of stay, and probable/definitive stent thrombosis (data available since 2010; Table 3).

Independent Predictors of In-Hospital Mortality in CS

In CS (n=4090), patients' age per additional year (OR, 1.04; 95% CI, 1.03–1.05), Charlson Comorbidity Index >1 (OR, 1.36; 95% CI, 1.09–1.70), and lack of PCI (OR, 2.80; 95% CI, 2.22–3.53) were independent predictors of in-hospital mortality; sex, STEMI, diabetes mellitus, hypertension, and dyslipidemia were not.

Analysis of the entire AMI population (n=51841; reference, no CS), CS at admission (OR, 43.1; 95% CI, 38.1–48.8; *P*<0.001), CS developing during in-hospital (OR, 36.8; 95% CI, 32.9–41.2; *P*<0.001), age per additional year (OR, 1.06; 95% CI, 1.06–1.07; *P*<0.001), STEMI (OR, 1.30; 95% CI, 1.18–1.43; *P*<0.001), and lack of PCI (OR, 3.05; 95% CI, 2.77–3.36; *P*<0.001) appeared as independent predictors of in-hospital mortality (Table 4).

DISCUSSION

In this analysis of a large, population-based registry covering 20 years of observation, rates of CS on admission increased during the last decade. In contrast, the trend of decreasing numbers of patients developing CS during hospitalization continued. Rates of PCI in CS further increased to 80% (2007–2017), compared with 40.2% in the previous time period of 1997 to 2006. Similarly, medical treatment with statins and P2Y12 inhibitors increased. Mortality declined from 62.2% in 1997 to <40% in 2017. We postulate that the increasing incidence of CS on admission is related to improvements in acute myocardial infarction network and medical care over the last 20 years leading to more frequent and rapid transportation of even sicker patients, who would otherwise have died before arriving at the hospital. In addition, the decreasing incidence of CS developed during hospitalization might be due to an earlier arrival at the hospital and an increased usage of PCI with reduction in infarct size.

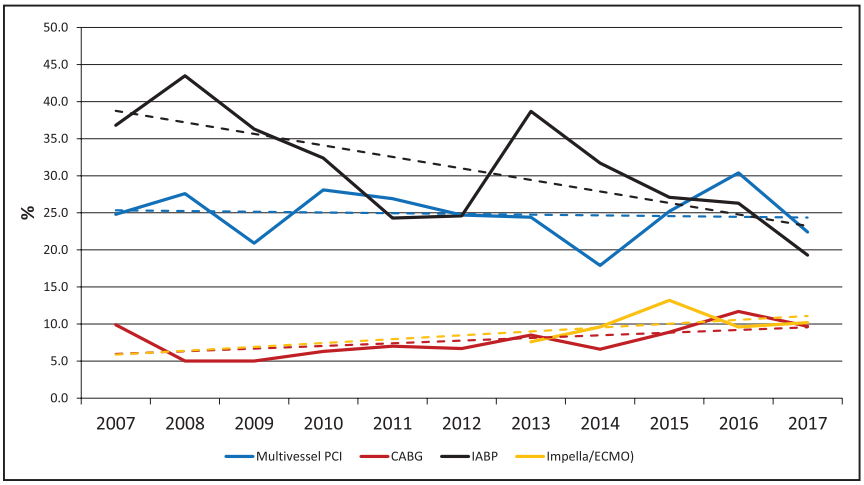

Figure 3. Trends in use of multivessel percutaneous coronary intervention (PCI); coronary artery bypass graft (CABG), intra-aortic balloon pump (IABP), and Impella/extracorporal membrane oxygenation (ECMO) in patients with acute myocardial infarction with cardiogenic shock.
Dotted lines indicate trendlines.

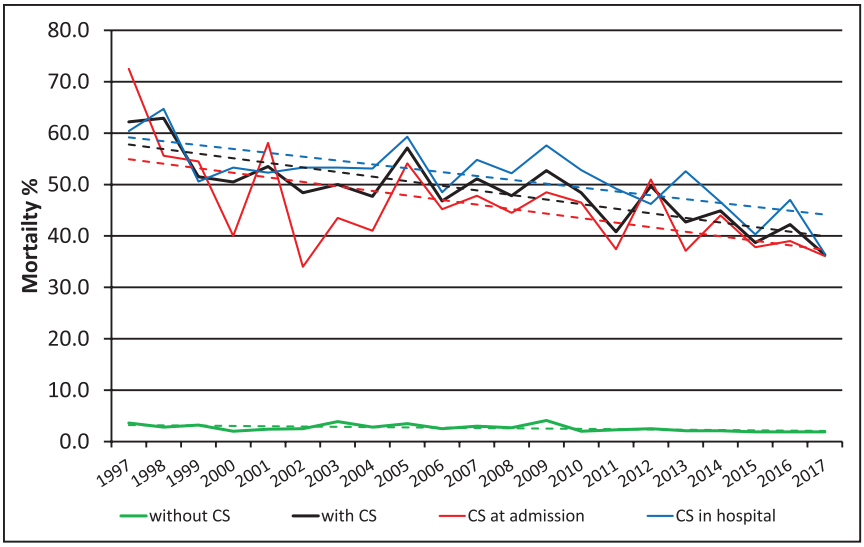

Figure 4. Trends in in-hospital mortality of patients with acute myocardial infarction according to cardiogenic shock (CS). Percentage in the table indicates percentage of overall CS. Dotted lines indicate trendlines.

Since the inclusion of multivessel intervention as parameter in the AMIS registry in 2003, the use of multivessel PCI in patients with CS and multivessel disease remained stable in approximately one-third of patients. We were unable to show a beneficial effect in terms of mortality among patients with CS undergoing multivessel PCI compared with culprit-only intervention. In the multivariable logistic regression model including only CS patients with multivessel disease (n=1225), multivessel PCI was not an independent predictor of in-hospital mortality (OR, 1.12). However, if patients with AMI and multivessel disease (n=15916) were analyzed together, multivessel PCI emerged as an independent predictor of in-hospital mortality with an OR of 1.88. Furthermore, AMI patients with multivessel disease and multivessel PCI, compared with culprit lesion–only PCI, more frequently developed CS during hospitalization (OR, 1.93). This finding is in line with the results of the CULPRIT-shock trial,[17] whereas higher mortality and need for renal replacement therapy was observed in the multivessel PCI group. Multivessel PCI in patients with AMI might even be one of the factors influencing the development of CS during hospitalization.

After publication of the IABP-shock II trial in 2012,[13] a numerical decrease in IABP use has been observed. In 2007 to 2013, 110 of 267 patients received an IABP (41.2%), whereas between 2014 and 2017, there were 37 of 96 patients who were treated with an IABP (38.5%; *P*=0.76). In parallel, there was an increased use of other mechanical circulatory devices such as vaECMO and Impella (Figure 3). Meanwhile, mortality declined from 47.3% in 2007 to 2013 (653 of 1380 patients) to 41.0% in 2014 to 2017 (305 of 743 patients; *P*=0.006). However, the collected data of vaECMO and axial flow pump (Impella) insertion in CS are incomplete. A detailed analysis is, therefore, not included in the current study, and we are not able to draw conclusion with respect to the influence of temporary mechanical circulatory devices on in-hospital mortality in recent years.

Independent predictors of in-hospital mortality remained unchanged compared with the previously analyzed period.[11] In the CS population, age, comorbidity (Charlson comborbidity index >1), and lack of PCI are associated with increased mortality. In the overall AMI population, predictors of mortality include CS (on

Table 3. Complications and Outcome in Hospital of Patients With Acute Myocardial Infarction

	No CS (n=47752)	CS (n=4090)	*P* Value	CS at Admission (n=1907)	CS During Hospitalization (n=2183)	*P* Value
Length of stay, d; median (IQR)	5 (2–9)	5 (1–13)	0.001	5 (1–12)	5 (1–15)	0.13
Reinfarction (%)	558/47721 (1.2)	288/4008 (7.2)	<0.001	56/1863 (3.0)	232/2145 (10.8)	<0.001
Bleeding, any (%)	932/33808 (2.8)	169/2552 (6.6)	<0.001	88/1533 (5.7)	81/1019 (7.9)	0.034
Cerebrovascular event (%)	326/47549 (0.7)	134/4015 (3.3)	<0.001	75/1863 (4.0)	59/2152 (2.7)	0.027
Mortality (%)	1268/47752 (2.7)	2014/4090 (49.2)	<0.001	847/1907 (44.4)	1167/2183 (53.5)	<0.001
MACE (%)	1924/47531 (4.0)	2089/3988 (52.4)	<0.001	880/1861 (47.3)	1209/2127 (56.8)	<0.001
Stent thrombosis (%), probable/definitive*	417/13506 (3.1)	33/1074 (3.1)	0.99	19/682 (2.8)	14/392 (3.6)	0.47

CS indicates cardiogenic shock; IQR, interquartile range; and MACE, major adverse cardiac event.
*Available since 2010.

Table 4. Multivariable Logistic Regression Analyses

Variables	OR	95% CI	*P* Value
CS at admission (no CS=reference)	43.1	38.1–48.8	<0.001
CS developing in hospital	36.8	32.9–41.2	<0.001
Age per additional year	1.06	1.06–1.07	<0.001
Female sex	1.04	0.95–1.14	0.42
STEMI	1.30	1.18–1.43	<0.001
No PCI	3.05	2.77–3.36	<0.001

Independent predictors of in-hospital mortality (n=51 841). CS indicates cardiogenic shock; OR, odds ratio; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

admission and developed during hospitalization), age, STEMI, and PCI.

Study Limitations

This study has several limitations.[11,20] The AMIS Plus Registry represents a high-risk cohort with an ST-segment–elevation AMI rate of >70%. Enrollment was not limited to patients with CS due to left ventricular failure but included all types of CS (eg, mechanical complication, right heart failure). As a general limitation of all registries, no central review of shock diagnoses was performed. However, CS was defined before the start of this registry.[19,21] These definitions were provided to the investigators in both the written and online case record forms, and the definitions used did not change during the study period. As with all nonrandomized data, we cannot exclude possible selection bias, confounding by indication, and residual confounding. No causal relationship can be established, and interactions among various residual unknown predictors of outcomes cannot be tested. Finally, follow-up time was limited to the hospital stay.

Conclusions

During the past decade, rates of CS on admission have increased, whereas rates of CS developing during hospitalization further decreased. Rates of revascularization by means of PCI have increased substantially from 40.2% in 1997 to 2006 to 80% in the time period of 2007 to 2017. Use of multivessel revascularization strategies in the CS population compared with culprit vessel–only PCI had no impact on in-hospital mortality in the CS population. However, multivessel PCI emerged as an independent predictor of in-hospital mortality and CS developing during hospitalization in the overall AMI population.

We can postulate that improvements in medical management, especially the increase of immediate PCI, relate to the observed reduction of CS development during hospitalization and the lower mortality rates among patients with CS in general.

Although a clear reduction of cardiogenic associated mortality was achieved in the last 20 years, fatal outcome remains high. There remains an important need for better therapeutic options and the need for randomized trials with respect of the utility of temporary mechanical circulatory device support.

ARTICLE INFORMATION

Received August 20, 2018; accepted January 30, 2019.

*A list of all AMIS Plus Registry Investigators is given in the Appendix.

Correspondence

Lukas Hunziker, MD, Department of Cardiology, Bern University Hospital, Bern, Switzerland. Email lukas.hunziker@insel.ch

Affiliations

Department of Cardiology, Bern University Hospital, Switzerland (L.H., T.P.). AMIS Plus Data Center, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Switzerland (D.R.). Division of Cardiology, University Hospital Basel, Switzerland (R.J.). Department of Cardiology, Cardiocentro Ticino, Lugano, Switzerland (G.P.). Heart Centre Lucerne, Luzerner Kantonsspital, Switzerland (F.C.). Cardiology Department, La Tour Hospital, Geneva, Switzerland (P.U.). Department of Biomedicine, University of Basel, Switzerland (P.E.). Department of Cardiology, Kantonsspital St. Gallen, Switzerland (H.R.).

Sources of Funding

The AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry is funded by unrestricted grants from the Swiss Heart Foundation and from Abbot AG, Amgen AG, AstraZeneca AG, Bayer (Switzerland) AG, B. Braun Medical AG, Biotronik AG, Cordis-Cardinal Health, Daiichi-Sankyo/Eli Lilly AG, A Menarini AG, Mepha Pharma AG, Merck Sharp & Dohme Chibret AG, Novartis Pharma Switzerland AG, Pfizer AG, Servier (Switzerland) AG, SIS Medical AG, St. Jude Medical, Vascular Medical AG, Working Group of Interventional Cardiology of the Swiss Cardiology Society. The sponsors did not play any role in the design, data collection, analysis, or interpretation of the registry.

Disclosures

Dr Jeger reports lecture honoraria and travel support from Braun. Dr Urban is a consultant to Biosensors Europe, Morges, Switzerland, and has received honoraria from Abbot Vascular, Edwards Life Sciences, and Terumo. Dr Rickli reports institutional research grants from Biotronik, Boston, Braun, Medtronic, and Terumo. Dr Pilgrim has received research grants to his institution from Edwards Lifesciences, Symetis, and Biotronik; has received speaker fees from Boston Scientific; and has received reimbursement for travel expenses from St. Jude Medical. The other authors report no conflicts.

APPENDIX

The AMIS Plus Registry Investigators are listed in alphabetic order with the names of the local principal investigators: Affoltern am Albis, Spital (F. Hess); Altdorf, Kantonsspital Uri (R. Simon); Altstätten, Spital (P.J. Hangartner); Baden, Kantonsspital (U. Hufschmid); Basel, St. Claraspital (B. Hornig/L. Altwegg); Basel, Universitätsspital (R. Jeger); Bern, Beau-Site Klinik (S. Trummler); Bern, Inselspital (S. Windecker, T. Pilgrim); Bern, Hirslanden Salem-Spital (T. Rueff); Bern, Tiefenauspital (P. Loretan); Biel, Spitalzentrum (C. Roethlisberger); Brig-Glis, Oberwalliser Kreisspital (D. Evéquoz); Bülach, Spital (G. Mang); Burgdorf, Regionalspital Emmental (D. Ryser); Chur, Rätisches Kantons- und Regionalspital (P. Müller); Chur, Kreuzspital (R. Jecker); Davos, Spital (W. Kistler); Dornach, Spital (T. Hongler); Einsiedeln, Regionalspital (S. Stäuble); Flawil, Spital (G. Freiwald); Frauenfeld Kantonsspital (H.P. Schmid); Fribourg, Hôpital cantonal (J.C. Stauffer/S. Cook); Frutigen, Spital (K. Bietenhard); Genève, Hôpitaux universitaires (M. Roffi); Glarus, Kantonsspital (W. Wojtyna); Grenchen, Spital (R. Schönenberger); Grosshöchstetten, Bezirksspital (C. Simonin); Heiden, Kantonales Spital (R. Waldburger); Herisau, Kantonales Spital (M. Schmidli); Horgen, See Spital (B. Federspiel); Interlaken, Spital (E.M. Weiss); Jegenstorf, Spital (H. Marty); Kreuzlingen, Herzzentrum Bodensee (K. Weber); La Chaux-de-Fonds,

Hôpital (H. Zender); Lachen, Regionalspital (I. Poepping); Langnau im Emmental, Regionalspital (A. Hugi); Laufenburg, Gesundheitszentrum Fricktal (E. Koltai); Lausanne, Centre hospitalier universitaire vaudois (J.F. Iglesias); Lugano, Cardiocentro Ticino (G. Pedrazzini); Luzern, Luzerner Kantonsspital (P. Erne, F. Cuculi); Luzern Klinik St. Anna (P. Erne); Männedorf, Kreisspital (T. Heimes); Martigny, Hôpital régional (B. Jordan); Mendrisio, Ospedale regionale (A. Pagnamenta); Meyrin, Hôpital de la Tour (P. Urban); Monthey, Hôpital du Chablais (P. Feraud); Montreux, Hôpital de Zone (E. Beretta); Moutier, Hôpital du Jura bernois (C. Stettler); Münsingen, Spital (F. Repond); Münsterlingen, Kantonsspital (F. Widmer); Muri, Kreisspital für das Freiamt (C. Heimgartner); Nyon, Group. Hosp. Ouest lémanique (R. Polikar); Olten, Kantonsspital (S. Bassetti); Rheinfelden, Gesundheitszentrum Fricktal (H.U. Iselin); Rorschach, Spital (M. Giger); Samedan, Spital Oberengadin (P. Egger); Sarnen, Kantonsspital Obwalden (T. Kaeslin); Schaffhausen, Kantonsspital (A. Fischer); Schlieren, Spital Limmattal (T. Herren); Schwyz, Spital (P. Eichhorn); Scuol, Ospidal d'Engiadina Bassa (C. Neumeier/G. Flury); Sion, Hôpital du Valais (G. Girod); Solothurn, Bürgerspital (R. Vogel); Stans, Kantonsspital Nidwalden (B. Niggli); St. Gallen, Kantonsspital (H. Rickli); Sursee, Luzerner Kantonsspital (S. Yoon, J. Nossen); Thun, Spital (U. Stoller); Thusis, Krankenhaus (U.P. Veragut); Uster, Spital (E. Bächli); Uznach, Spital Linth (A. Weber); Walenstadt, Kantonales Spital (D. Schmidt/J. Hellermann); Wetzikon, GZO Spital (U. Eriksson); Winterthur, Kantonsspital (T. Fischer); Wolhusen, Luzener Kantonsspital (M. Peter); Zofingen, Spital (S. Gasser); Zollikerberg, Spital (R. Fatio); Zug, Kantonsspital (M. Vogt/D. Ramsay); Zürich, Hirslanden Klinik (C. Wyss); Zürich, Hirslanden Klinik im Park (O. Bertel); Zürich, Universitätsspital (M. Maggiorini); Zürich, Stadtspital Triemli (F. Eberli); Zürich, Stadtspital Waid (S. Christen).

REFERENCES

1. Kalmanovich E, Blatt A, Brener S, Shlezinger M, Shlomo N, Vered Z, Hod H, Goldenberg I, Elbaz-Greener G. Trends in the management and outcomes of patients admitted with acute coronary syndrome complicated by cardiogenic shock over the past decade: Real world data from the acute coronary syndrome Israeli survey (ACSIS). *Oncotarget*. 2017;8:42876–42886. doi: 10.18632/oncotarget.17152
2. Redfors B, Angerås O, Råmunddal T, Dworeck C, Haraldsson I, Ioanes D, Petursson P, Libungan B, Odenstedt J, Stewart J, Lodin E, Wahlin M, Albertsson P, Matejka G, Omerovic E. 17-year trends in incidence and prognosis of cardiogenic shock in patients with acute myocardial infarction in western Sweden. *Int J Cardiol*. 2015;185:256–262. doi: 10.1016/j.ijcard.2015.03.106
3. Abdel-Qadir HM, Ivanov J, Austin PC, Tu JV, Dzavík V. Temporal trends in cardiogenic shock treatment and outcomes among Ontario patients with myocardial infarction between 1992 and 2008. *Circ Cardiovasc Qual Outcomes*. 2011;4:440–447. doi: 10.1161/CIRCOUTCOMES.110.959262
4. Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation*. 2009;119:1211–1219. doi: 10.1161/CIRCULATIONAHA.108.814947
5. Goldberg RJ, Makam RC, Yarzebski J, McManus DD, Lessard D, Gore JM. Decade-long trends (2001-2011) in the incidence and hospital death rates associated with the in-hospital development of cardiogenic shock after acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2016;9:117–125. doi: 10.1161/CIRCOUTCOMES.115.002359
6. Nguyen HL, Yarzebski J, Lessard D, Gore JM, McManus DD, Goldberg RJ. Ten-year (2001–2011) trends in the incidence rates and short-term outcomes of early versus late onset cardiogenic shock after hospitalization for acute myocardial infarction. *J Am Heart Assoc*. 2017;6:e005566. doi: 10.1161/JAHA.117.005566
7. De Luca L, Olivari Z, Farina A, Gonzini L, Lucci D, Di Chiara A, Casella G, Chiarella F, Boccanelli A, Di Pasquale G, De Servi S, Bovenzi FM, Gulizia MM, Savonitto S. Temporal trends in the epidemiology, management, and outcome of patients with cardiogenic shock complicating acute coronary syndromes. *Eur J Heart Fail*. 2015;17:1124–1132. doi: 10.1002/ejhf.339
8. Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, Jain D, Gotsis W, Ahmed A, Frishman WH, Fonarow GC. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc*. 2014;3:e000590. doi: 10.1161/JAHA.113.000590
9. Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, Jain D, Cooper HA, Frishman WH, Menon V, Bhatt DL, Abbott JD, Fonarow GC, Panza JA. Trends in coronary angiography, revascularization, and outcomes of cardiogenic shock complicating non-ST-elevation myocardial infarction. *Am J Cardiol*. 2016;117:1–9. doi: 10.1016/j.amjcard.2015.10.006
10. Babaev A, Frederick PD, Pasta DJ, Every N, Sichrovsky T, Hochman JS; NRMI Investigators. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA*. 2005;294:448–454. doi: 10.1001/jama.294.4.448
11. Jeger RV, Radovanovic D, Hunziker PR, Pfisterer ME, Stauffer JC, Erne P, Urban P; AMIS Plus Registry Investigators. Ten-year trends in the incidence and treatment of cardiogenic shock. *Ann Intern Med*. 2008;149:618–626.
12. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, de Waha A, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Lauer B, Böhm M, Ebelt H, Schneider S, Werdan K, Schuler G; Intraaortic Balloon Pump in cardiogenic shock II (IABP-SHOCK II) Trial Investigators. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. *Lancet*. 2013;382:1638–1645. doi: 10.1016/S0140-6736(13)61783-3
13. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebelt H, Schneider S, Schuler G, Werdan K; IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296. doi: 10.1056/NEJMoa1208410
14. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119–177. doi: 10.1093/eurheartj/ehx393
15. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Ting HH, O'Gara PT, Kushner FG, Ascheim DD, Brindis RG, Casey DE Jr, Chung MK, de Lemos JA, Diercks DB, Fang JC, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation*. 2016;133:1135–1147. doi: 10.1161/CIR.0000000000000336
16. Patel MR, Calhoon JH, Dehmer GJ, Grantham JA, Maddox TM, Maron DJ, Smith PK. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2016 appropriate use criteria for coronary revascularization in patients with acute coronary syndromes: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and the Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2017;69:570–591. doi: 10.1016/j.jacc.2016.10.034
17. Thiele H, Akin I, Sandri M, Fuernau G, de Waha S, Meyer-Saraei R, Nordbeck P, Geisler T, Landmesser U, Skurk C, Fach A, Lapp H, Piek JJ, Noc M, Goslar T, Felix SB, Maier LS, Stepinska J, Oldroyd K, Serpytis P, Montalescot G, Barthelemy O, Huber K, Windecker S, Savonitto S, Torremante P, Vrints C, Schneider S, Desch S, Zeymer U; CULPRIT-SHOCK Investigators. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl J Med*. 2017;377:2419–2432. doi: 10.1056/NEJMoa1710261
18. Schoenenberger AW, Radovanovic D, Windecker S, Iglesias JF, Pedrazzini G, Stuck AE, Erne P; AMIS Plus Investigators. Temporal trends in the treatment and outcomes of elderly patients with acute coronary syndrome. *Eur Heart J*. 2016;37:1304–1311. doi: 10.1093/eurheartj/ehv698
19. Killip T III, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol*. 1967;20:457–464.
20. Radovanovic D, Erne P. AMIS Plus: Swiss registry of acute coronary syndrome. *Heart*. 2010;96:917–921. doi: 10.1136/hrt.2009.192302
21. Califf RM, Bengtson JR. Cardiogenic shock. *N Engl J Med*. 1994;330:1724–1730. doi: 10.1056/NEJM199406163302406